

REMARKS

Claims 1, 3, 4, 7-17, 22, 23, and 27 are pending in the application. Claims 2, 5, 6, 18-21, 24-26, and 28-42 have been cancelled without prejudice. Claims 1 and 17 have been amended. Support for the amendments can be found in original claims 2, 5, 6, and 18-21 and in the specification at, e.g., page 5, lines 15-28, and page 21, lines 25-28. These amendments add no new matter.

Rejoinder

At page 2 of the Office Action, the Examiner stated that claims 23-42 have been withdrawn from consideration as being drawn to non-elected subject matter. Claims 24-26 and 28-42 have been cancelled without prejudice. Claim 23 is directed to a method of identifying a compound that prevents or suppresses alpha-synuclein-induced toxicity. Claim 27 is directed to a method of identifying an extragenic suppressor of alpha-synuclein-induced toxicity. Method claims 23 and 27 depend from and include all of the limitations of composition claim 1. In accordance MPEP § 821.04, applicants request that the Examiner rejoin and examine method claims 23 and 27 upon the allowance of composition claim 1.

Priority

At pages 2-3 of the Office Action, the Examiner stated that claim 16 is entitled to a priority date of April 16, 2004 (the filing date of the present application). In view of the amendments and remarks presented herein, applicants respectfully submit that examination of the present application does not require a determination of whether claim 16 is also entitled to the priority dates of application serial number 60/463,284, filed April 16, 2003 and application serial number 60/472,317, filed May 20, 2003.

Claim Objections

At page 3 of the Office Action, claim 1 was objected to in its recitation of the phrase "such that induction of production of the protein is toxic to the yeast cell." Claim 1 has been

amended to recite "wherein induction of production of the protein is toxic to the yeast cell." It is applicants' understanding that this amendment obviates the present objection.

35 U.S.C. § 112, First Paragraph (Enablement)

At pages 3-7 of the Office Action, claims 1-23 were rejected as not enabled. According to the Office Action, "the specification, while being enabling for a yeast cell comprising protein or nucleic acid comprising alpha-synuclein wherein the alpha-synuclein is wild-type alpha synuclein or mutant A53T and wherein the cell comprises two integrated copies of the expression construct, does not reasonably provide enablement for any other embodiment."

Independent claims 1 and 17 have each been amended to require that the claimed yeast cell contain two integrated copies of an expression construct comprising a nucleic acid encoding a protein comprising wild-type human alpha-synuclein or mutant human alpha-synuclein A53T. It is applicants' understanding that these amendments obviate the present objection.

35 U.S.C. § 102(e) (Anticipation)

At pages 7-8 of the Office Action, claims 1, 3, 4, 5, 6, 9, 11, 12, 17, 18, 20, and 21 were rejected as anticipated by Kim et al., U.S. Patent No. 6,858,704 ("Kim") as evidenced by Lindquist et al., U.S. Patent No. 7,045,290 ("Lindquist").

Independent claims 1 and 17 have each been amended to incorporate the limitations of dependent claims 2 and 19 (which dependent claims were not rejected under the present heading). It is applicants' understanding that these amendments obviate the present objection.

At pages 8-9 of the Office Action, claims 1-15 and 17-22 were rejected as anticipated by Lindquist.

Amended independent claims 1 and 17 are directed to yeast cells that, among other features recited in the claims, comprise two integrated copies of an expression construct comprising a nucleic acid encoding a protein comprising wild-type human alpha-synuclein or mutant human alpha-synuclein A53T. As detailed in the present application, the inventors have

discovered that alpha-synuclein-induced toxicity in yeast is dosage dependent. Yeast cells that contain one integrated copy of an alpha-synuclein gene under the regulation of a galactose-inducible promoter showed moderate growth defects whereas cells with two copies exhibited extreme defects (see specification at page 2, lines 16-25 and page 40, line 20, to page 41, line 3).

Lindquist discloses that expression of wild-type human alpha-synuclein or mutant human alpha-synuclein A53T in yeast is toxic to the cells. However, Lindquist does not describe yeast cells containing two integrated copies of a construct encoding alpha-synuclein, as is required by the claims of the present application. The Office Action cited column 21 of Lindquist as describing vectors that "allow integration of two copies or more as recited in claims 2 and 19." However, column 21 of Lindquist does not describe construction of the cells used by Lindquist in the experiments depicted in Figure 3. Furthermore, the section in column 21 entitled "Integrating plasmids" describes an exemplary plasmid (Y1p) that is maintained at one copy per haploid genome (see column 21, lines 11-13). Column 21 of Lindquist contains extensive description of many types of nucleic acid vectors (many of which are autonomously replicating vectors) that can be used for expression of proteins identified by the generic term "misfolded disease protein." There is no description in column 21 of preparation of a yeast cell that contains two integrated copies of an expression construct encoding alpha-synuclein. As a result, Lindquist does not anticipate independent claims 1 or 17 or the claims that depend therefrom. Applicants respectfully request that the Examiner withdraw the rejection.

35 U.S.C. § 103(a) (Obviousness)

At pages 9-10 of the Office Action, claim 16 was rejected as unpatentable over Lindquist in view of Frate, U.S. Published Application No. 20040115792.

Claim 16 depends from claim 14 (which depends from independent claim 1) and requires that the claimed yeast cell contain a disruption in the PDR5 gene.

The Office Action cited Frate as describing "use of a yeast cell line comprising a disruption of PDR5 for testing genotoxicity and cytotoxicity of environmental contaminants." As detailed above in response to the anticipation rejection, Lindquist does not disclose the yeast

cell of independent claim 1. Frate provides nothing that supplements the deficiencies of Lindquist or renders obvious independent claim 1. Accordingly, once independent claim 1 is held allowable, dependent claim 16 should also be in condition for allowance.

CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are in condition for allowance, which action is requested.

Enclosed is a Petition for Three Month Extension of Time. The extension of time fee in the amount of \$510 is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply other any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 17481-003001.

Respectfully submitted,

Date: September 26, 2007



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